Figure 1A

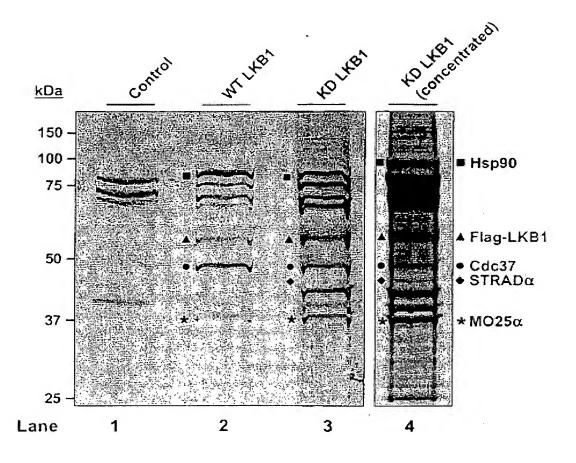


Figure 1B

	Protein name	Peptide matches	% sequence coverage	NCBI gi number	
*	Hsp90	15/44	30%	20149594	
A	Flag-LKB1	14/46	35%	7106425	
•	Cdc37	31/72	59%	5901922	
•	STRADα	11/80	34%	12060855	
*	ΜΟ25α	17/37	47%	7706481	

Figure 1C

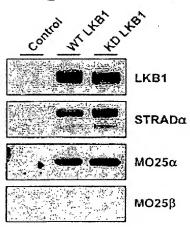


Figure 2A

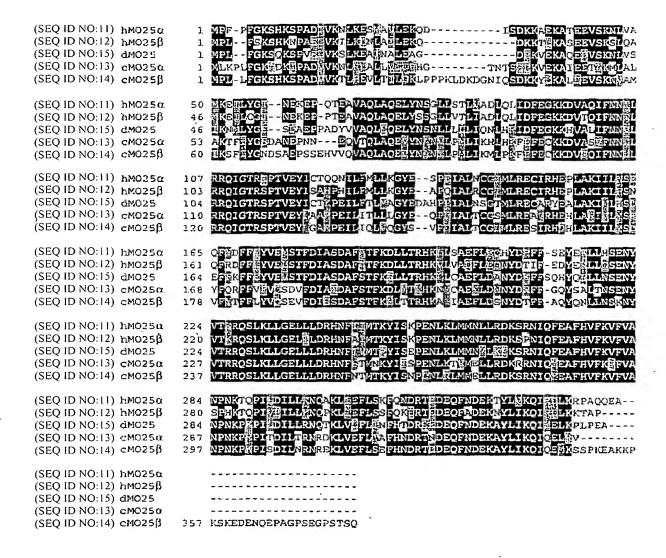


Figure 2B

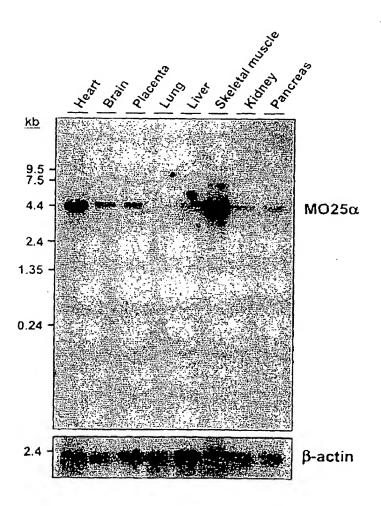


Figure 2C

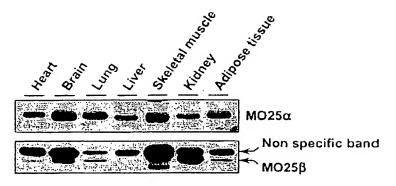
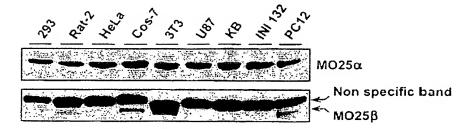


Figure 2D





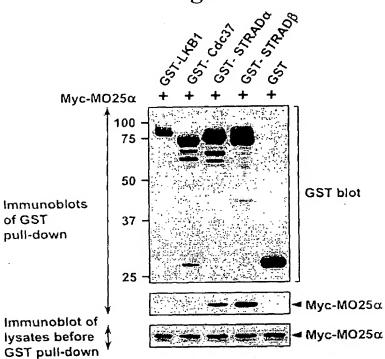


Figure 4B

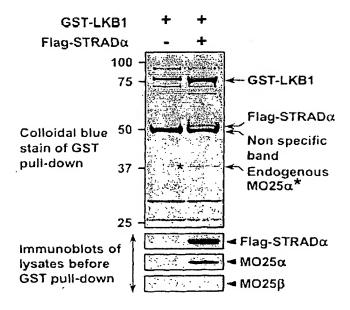


Figure 4C

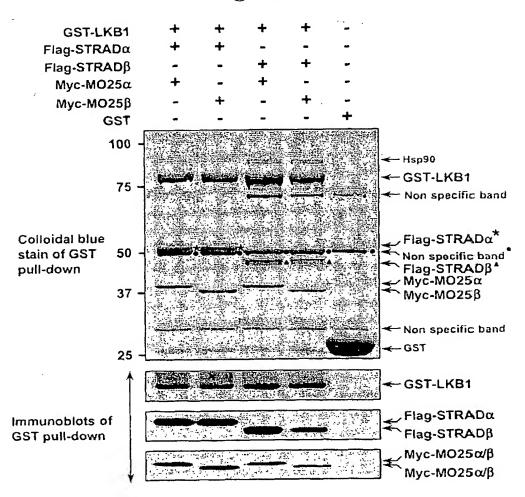


Figure 5 (continued)

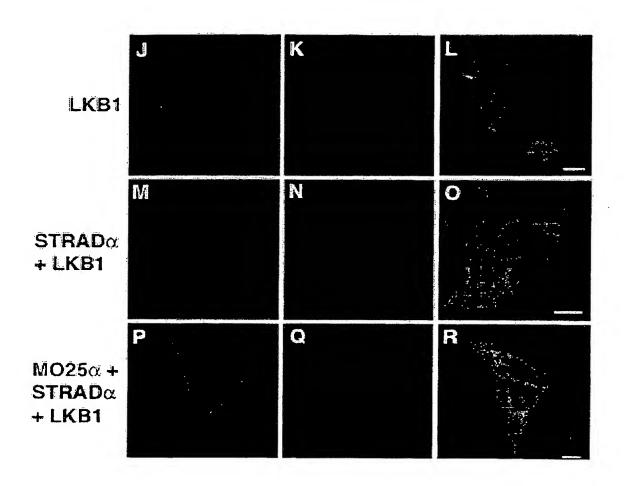


Figure 6A

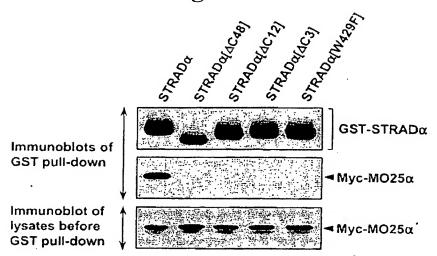


Figure 6B

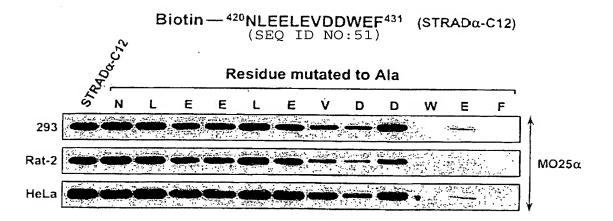


Figure 6C

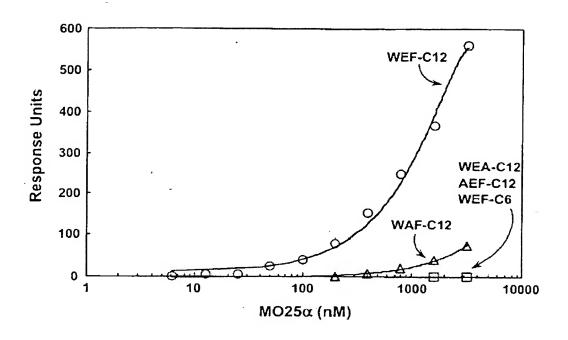


Figure 10

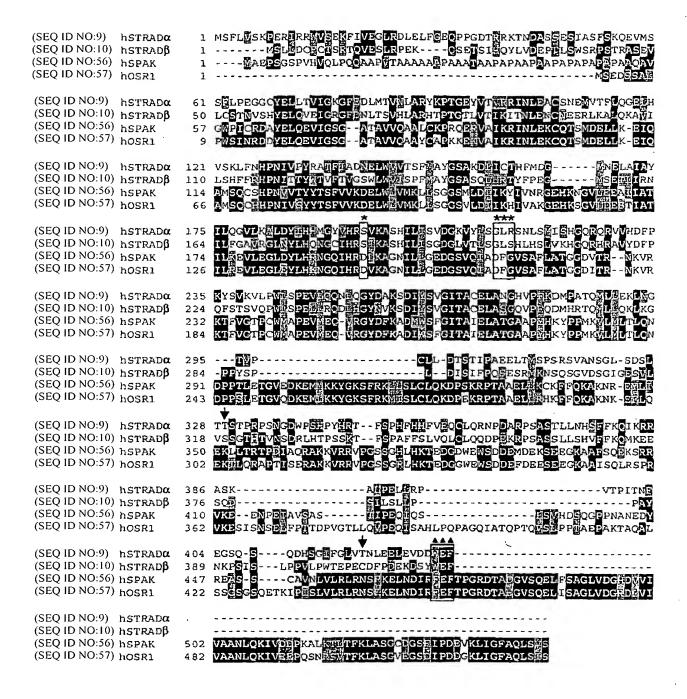


Figure 12

```
11 ...LPRSSLLYNNASNSSSRIKETRKVKLLYNPLTKR.....Q...ILNNFEILATLGNGO
(SEQ ID NO:58) Tos3
                      94 ..TPTTTSSFCSSGSSKNKVEETNRISLTYDPVSKR....K...VLNTYEIIKELGHGQ
(SEQ ID NO:59) Pak1
                     121 CICPSLPYSPVSSPQSSPRLPRRPTVESHHVSITGM.....QDCVQLNQYTLKDEIGKGS
(SEQ ID NO:61) Camkkß
                       7 OOLGMFTEGELMSVGMDTFIHRIDSTEVIYQP..RR....KRAKLIGKYLMGDLLGEGS
(SEQ ID NO:6) LKB1
                      39 TSSFGSSFSQQKPTYSTIIGENIHTILDEIRPYVKKITVSDQDKKTINQYTLGVSAGSGQ
(SEO ID NO:60) Elml
                                                  tv l y pltkr
                                                                        ilony i
                                    s ss rik
(SEQ ID NO:62) consensus 121
                            p ss s
                       61 YGKVKLARDIGTGALVAIKILNRFEKRS....GYSL.....QLKV.EN......
(SEO ID NO:58) Tos3
                     144 HGKVKLARDILSKQLVAIKIVDRHEKKQRKFFTFIK.....SSKISEN......
(SEQ ID NO:59) Pak1
                     176 YGVVKLAYNENDNTYYAMKVLSK..KKLIRQAGFPR......RPPPRGTRPAPGGCIQP
(SEQ ID NO:61) Camkkß
(SEQ ID NO:6) LKB1
                       60 YGKVKEVLDSETLCRRAVKILKK..KKLRR......I
                      99 FGYVRKAYSSTLGKVVAVKIIPKKPWNAQQYSVNQVMRQIQLWKSKGKITTNMSGNEAMR
(SEQ ID NO:60) Elml
(SEQID NO:62) consensus 181 yGkVkla d t lvAiKil k kk k y
                      99 ....PRVNQEIEVMKRCHHE.NVVELYEILNDPESTKVYLVLEYCSRGPVKWCPENKMEI
(SEQ ID NO:58) Tos3
                     187 ....DKIKREIAIMKKCHHK.HVVQLIEVLDDLKSRKIYLVLEYCSRGEVKWCPPDCMES
(SEQ ID NO:59) Pak1
                     227 RGPIEQVYQEIAILKKLDHP.NVVKLVEVLDDPNEDHLYMVFELVNQGPV.....MEV
(SEQ ID NO:61) CamkkB
(SEQ ID NO:6) LKB1
                      89 PNGEANVKKEIOLLRRLRHK.NVIQLVDVLYNEEKQKMYMVMEYC.....VCGMQEM.L
                      159 LMNIEKCRWEIFAASRLRNNVHIVRLIECLDSPFSESIWIVTNWCSLGELQWKRDDDEDI
(SEQ ID NO:60) Elml
                              drvk EI vmkrlhh nvv LievLddp s kvylVleycs g v wc
(SEQ ID NO:62) consensus 241
                     154 .KAVGPSILTFQQ....SRKVVLDVVSGLEYLHSQGITHRDIKPSNLLISSNGTV.KISD
(SEQ ID NO:58) Tos3
                     242 .DAKGPSLLSFQE....TREILRGVVLGLEYLHYQGIIHRDIKPANLLISGDGTV.KISD
(SEQ ID NO:59) Pak1
                     279 .PTLKP..LSEDQ....ARFYFQDLIKGIEYLHYQKIIHRDIKPSNLLVGEDGHI.KIAD
(SEQ ID NO:61) Camkkβ
(SEQ ID NO:6) LKB1
                     141 .DSVPEKRFPVCQ....AHGYFCQLIDGLEYLHSQGIVHKDIKPGNLLLTTGGTL.KISD
                     219 LPQWKKIVISNCSVSTFAKKILEDMTKGLEYLHSQGCIHRDIKPSNILLDEEEKVAKLSD
(SEQ ID NO:60) Elm1
                                           ar vv dvv GlEYLHsQgiiHrDIKPsNlLis dgtv KisD
(SEQ ID NO:62) consensus 301
                             v p ils q
                      208 FG..VAM.STATGSTNIQSSHEQLLKSRALGTPAFFAPELCSTEKEY.....
(SEQ ID NO:58) Tos3
                     296 FG..VSLAASSTNSSDSSESLDELELAKTVGTPAFFAPEMCLGEDAFTRYNLTKENLFRG
(SEQ ID NO:59) Pak1
                     331 FG..V.....SNEFKGS..DALLSNTVGTPAFMAPESLS.....ETRKIFSG
(SEQ ID NO:61) Camkkβ
(SEQ ID NO:6) LKB1
(SEQ ID NO:60) Elm1
                     195 LG..VAEALHPFAADDTCRTSQ......GSPAFQPPEIANGLDTFS.....
                     279 FGSCIFTPQSLPFSDANFEDCFQRELNKIVGTPAFIAPELCHLGNSKRDFVTD......
(SEQ ID NO:62) consensus 361 fG v
                                  t
                                       s d
                                            S
                                                   l r vGtPAF aPElc
                      252 SC.SSAIDIWSLGVTIYCLLFGKLPFNANSGLELFDSIINKPLEFPSYEEMLNGATSGIT
(SEQ ID NO:58) Tos3
                      354 SCISFMIDIWAVGVTLYCLLFGMLPFFSDFELKLFEKIVNDPLKFPTFKEIQSNKVSKVS
(SEQ ID NO:59) Pak1
(SEQ ID NO:61) Camkkβ
                     369 K....ALDVWAMGVTLYCFVFGQCPFMDERIMCLHSKIKSQALEFPDQPDIA......
                      233 ...GFKVDIWSAGVTLYNITTGLYPFEGDNIYKLFENIGKGSYAIP......
(SEQ ID NO:6) LKB1
                     332 ...GFKLDIWSLGVTLYCLLYNELPFFGENEFETYHKIIEVSLSSKINGNTLNDLVIKRL
(SEQ ID NO:60) Elm1
                              f iDiWslGVTlYcllfg lPF ad 1 lfdkIi
(SEQ ID NO:62) consensus 421
                      311 M.EEYT...DAKDLLKKLLQKDPDKRIKLADIKVHPFMC....HYGKSDAASVL...TN
(SEQ ID NO:58) Tos3
                      414 CEEEYE...MAKDLLLKLLEKNPQKRMTIPAIKKHPFVS.WDFDHVPENDEKLLS...SV
(SEQ ID NO:59) Pak1
                      417 ....E...DLKDLITRMLDKNPESRIVVPEIKLHPWVTRHGAEPLFSEDENCTLVEVTE
(SEQ ID NO:61) CamkKB
                      276 .GDCGP...PLSDLLKGMLEYEPAKRFSIRQIRQHSWFRK...KHPPAEAPVPIPPSPDT
(SEQ ID NO:6) LKB1
                     389 LEKDVTLRISIQDLVKVLSRDQPIDSRNHSQISSSS.VNPVRNEGPVRRFFGRLLTKKGK
(SEQ ID NO:60) Elml
(SEQ ID NO:62) consensus 481
                                    lkDLlkklleknP kri l Ik hpfv
                                                                      dh p d
                      359 LETFHELKVSPP......SSCKRVELVSLPVNSSFASLDSVYMENFOHNNLRTGADRNS
(SEQ ID NO:58) Tos3
                      467 LE..QKLRF......QCNQTDQFE.PISISKHELKNAV.....SGVGKKIKESV
(SEQ ID NO:59) Pakl
                      469 EEVENSVKHIPSLATVILVKTMIRKRSFGNPFEGSRREERSLSAPGNLLTKQGSEDNLOG
(SEQ ID NO:61) Camkkβ
                     329 KDRWRSMTVVPYLEDLHGADEDEDLFDIEDDIIYTQDFTVPGQVPEEEASHNGQRRGLPK
(SEQ ID NO:6) LKB1 ·
                      448 KKTSGKGKDKVLVSATSKVTPSIHIDEEPDKECFSTTVLRSSPDSSDYCSSLGEEAIQVT
(SEQ ID NO:60) Elm1
                                                        pv s
                                                               lks
                                lk pl
                                                 rve
(SEQ ID NO:62) consensus 541 e
```

Figure 15A $\label{eq:figure 15A}$ Activation of AMPKlpha1 catalytic domain by LKB1

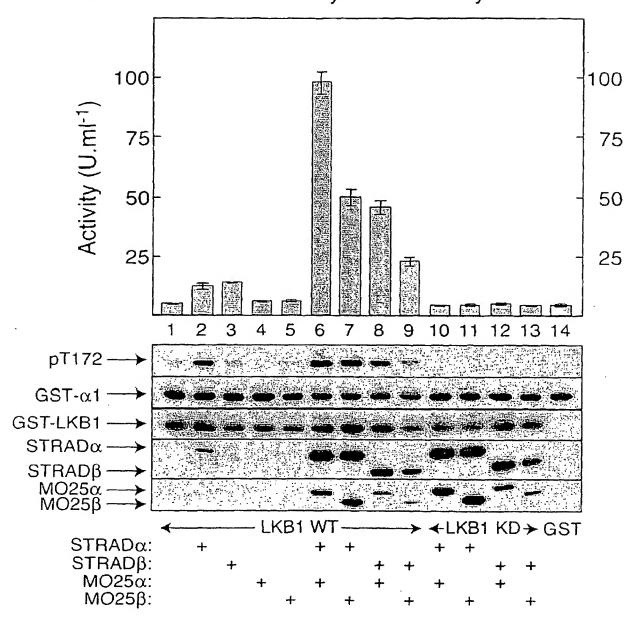


Figure 15B

Phosphorylation of AMPK α 1 catalytic domain by LKB1

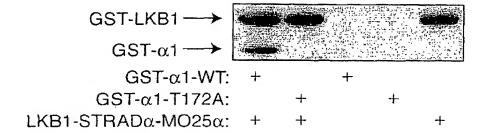


Figure 19

			-11 -12 -10-9 -5 -3 -2 P
			\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\
(SEQ ID NO:63)	ΡΚΑ-Cα	239	DFGFAKRV.KG.RTWTLCGTPEYLAPE
(SEQ ID NO:64)	ΡΚΟα	539	${\tt DFGM}{\tt CKEHMM.DGVTTR}{\tt TFCGTPDYIAPE}$
(SEQ ID NO:65)	NuaK1	196	${\tt DFGLSNL}{\tt YQKDKFLQTFCGSPLYASPE}$
(SEQ ID NO:66)	NuaK2	237	${\tt DFGLSNL}{\tt YHQGKFLQTFCGSPLYASPE}$
(SEQ ID NO:67)	BrsK1	190	${\tt DFGMA} {\tt SL} {\tt QVGDSLLETSCGSPHYACPE}$
(SEQ ID NO:68)	BrsK2	1′59	${\tt DFGMASL} {\tt QVGDSLLETSCGSPHYACPE}$
(SEQ ID NO:69)	SIK	167	${\tt DFG}{\tt FGNF}{\tt YKSGEPLSTWCGSPPYAAPE}$
(SEQ ID NO:70)	QIK	160	DFGFGNFFKSGELLATWCGSPPYAAPE
(SEQ ID NO:71)	AtSnRK1-α1	160	DFGLSNIMRDGHFLKTSCGSPNYAAPE
(SEQ ID NO:72)	AtSnRK1-α2	161	${\tt DFGLSNVMRDGHFLKTSCGSPNYAAPE}$
(SEQ ID NO:73)	AMPK-α1	159	DFGLSNMMSDGEFLRTSCGSPNYAAPE
(SEQ ID NO:74)	AMPK-α2	157	DFGLSNMMSDGEFLRTSCGSPNYAAPE
(SEQ ID NO:75)	ScSnf1	195	DFGLSNIMTDGNFLKTSCGSPNYAAPE
(SEQ ID NO:76)	QSK	206	DFGFSNLFTPGQLLKTWCGSPPYAAPE
(SEQ ID NO:77)	MELK	150	DFGLCAKPKGNKDYHLQTCCGSLAYAAPE
(SEQ ID NO:78)	consensus	243	DFGlsnl g fL TsCGSp YAaPE

Figure 21A

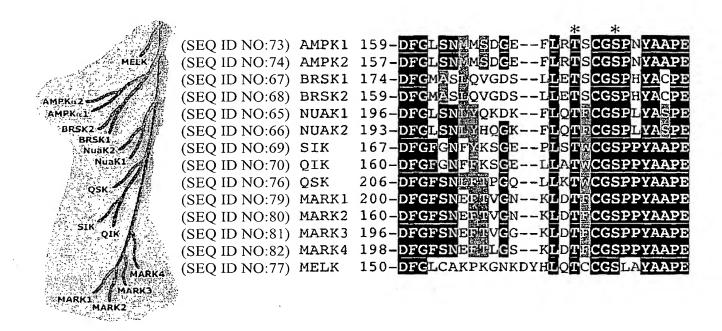


Figure 21B

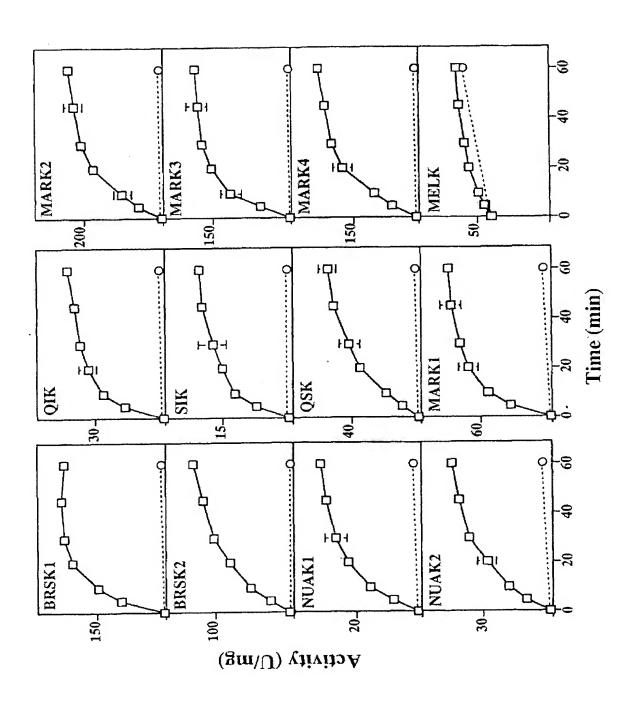
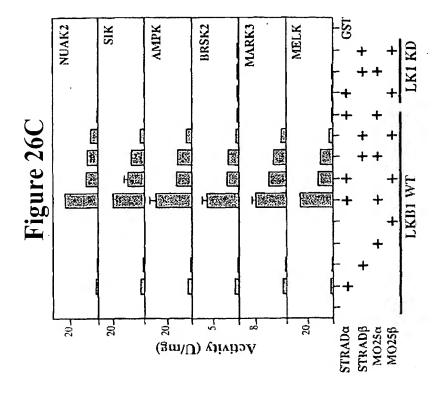
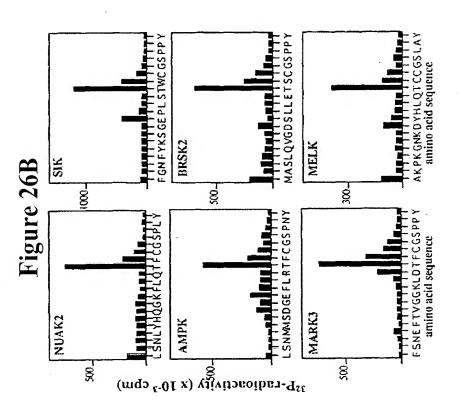
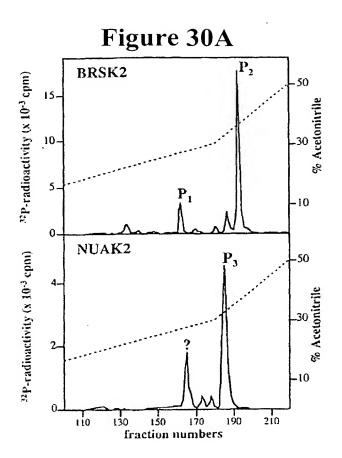


Figure 26A

	When the second	With the same of t	17 / 18	X7 (T1/)	Z) (X
	Peptide		Nm (mlvI)	Nm (MIVI) V max (U/Mg) V max/Nm	v max/ In m
NUAK2	LSNLYHQGKFLQTFCGSPLYRRR (SEQ ID NO:83) 0.15 ± 0.02	(SEQ ID NO:83)	0.15 ± 0.02	86.8 ± 3.4	578
SIK	FGNFYKSGEPLSTWCGSPPYRRR (SEQ ID NO:84) 0.46 ± 0.05	(SEQ ID NO:84)	0.46 ± 0.05	63.9 ± 2.2	139
AMPK	LSNMMSDGEFLR $\underline{\mathbf{r}}$ SCGSPNYRRR (SEQ ID NO:85) 1.40 ± 0.24	(SEQ ID NO:85)	1.40 ± 0.24	94.1 ± 8.3	19
BRSK2	MASLQVGDSLLETSCGSPHYRRR (SEQ ID NO:86)	(SEQ ID NO:86)	0.40 ± 0.06	10.6 ± 0.6	26
MARK3	FSNEFTVGGKLD <u>T</u> FCGSPPYRRR (SEQ ID NO:87) 0.62 ± 0.06	(SEQ ID NO:87)	0.62 ± 0.06	10.2 ± 0.4	91
MELK	AKPKGNKDYHLQ <u>I</u> CCGSLAYRRR (SEQ ID NO:88)	(SEQ ID NO:88)	₹	09×	







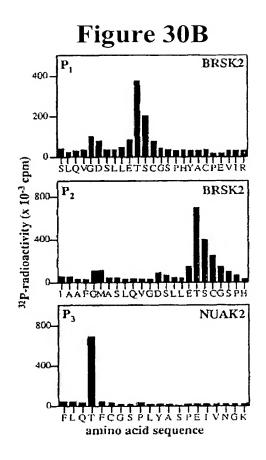


Figure 30C

Kinase	Posphopeptide		Mass observed	Theoretical mass
BRSK2 P,	IAAFGmASLQVGDSLLET(p)SCGSPHYACPEVIR	(SEQ ID NO:89)	3268.7870	3628.6680
BRSK2 P ₂	SLQVGDSLLET(p)SCGSPHYACPEVIR	(SEQ ID NO:90)	2951.4530	2951.3472
NUAK2 P	FLQT(p)FCGSPLYASPEIVNGK	(SEQ ID NO:91)	2356.1088	2356.1333
MARK4	LDT(p)FCGSPPYAAPELFQGK	(SEQ ID NO:92)	2225.9983	2226.1497
MELK	GNKDYHLQT(p)CCGSLAYAAPELIQCK	(SEQ ID NO:93)	2970.4421	2970.3648